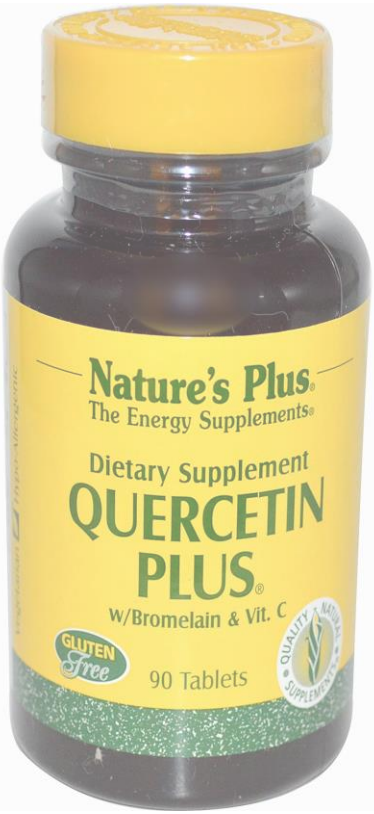

In The Name Of
GOD

The benefits of quercetin and features



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Supervisor: Dr. Gheibi

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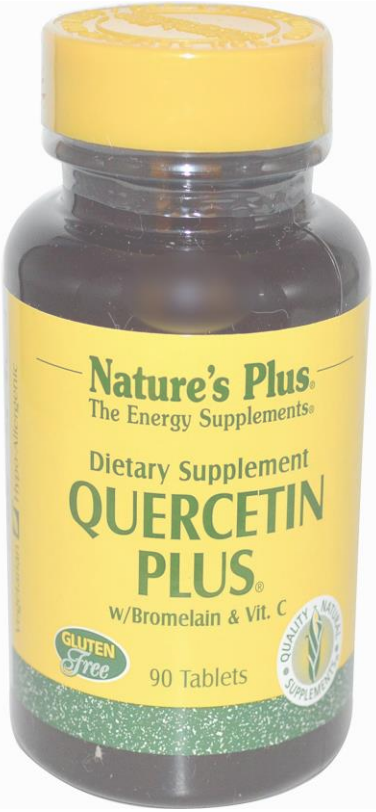
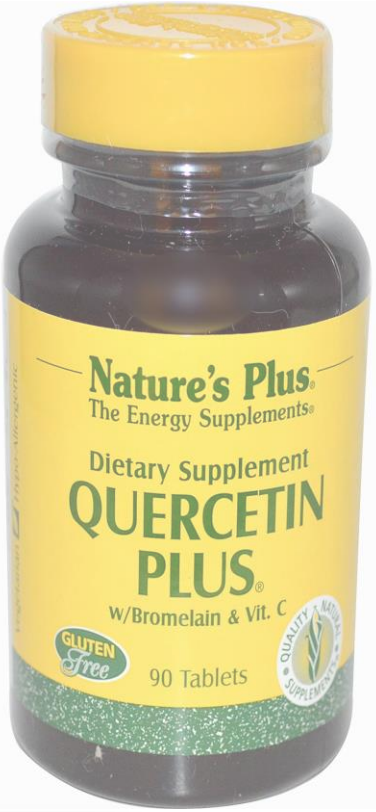
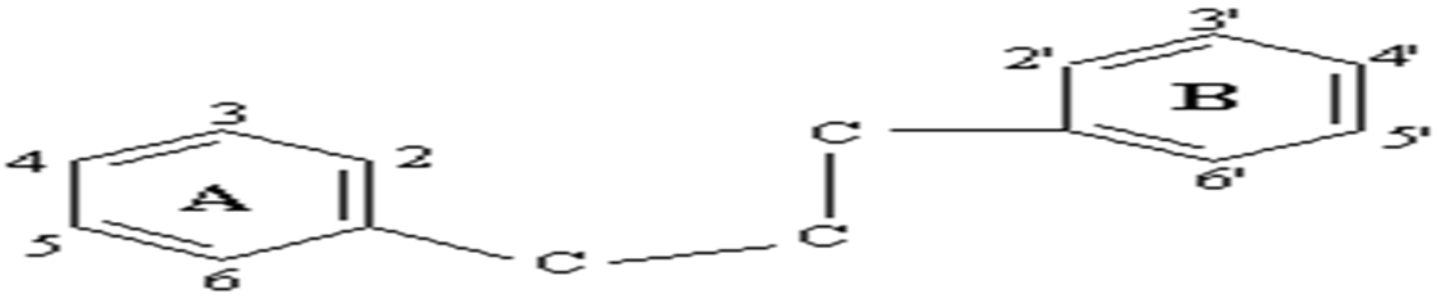


FLAVONOIDS

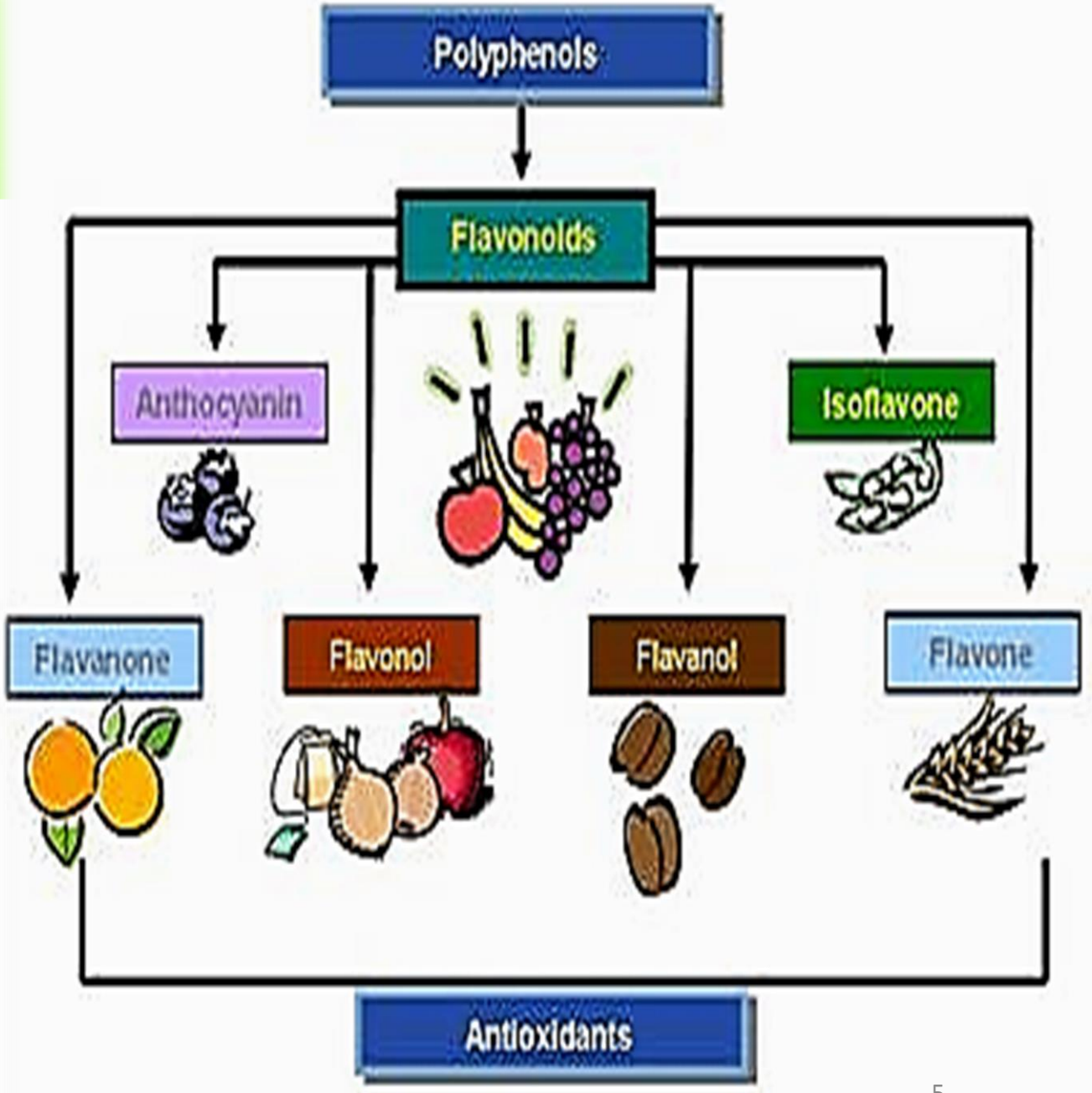


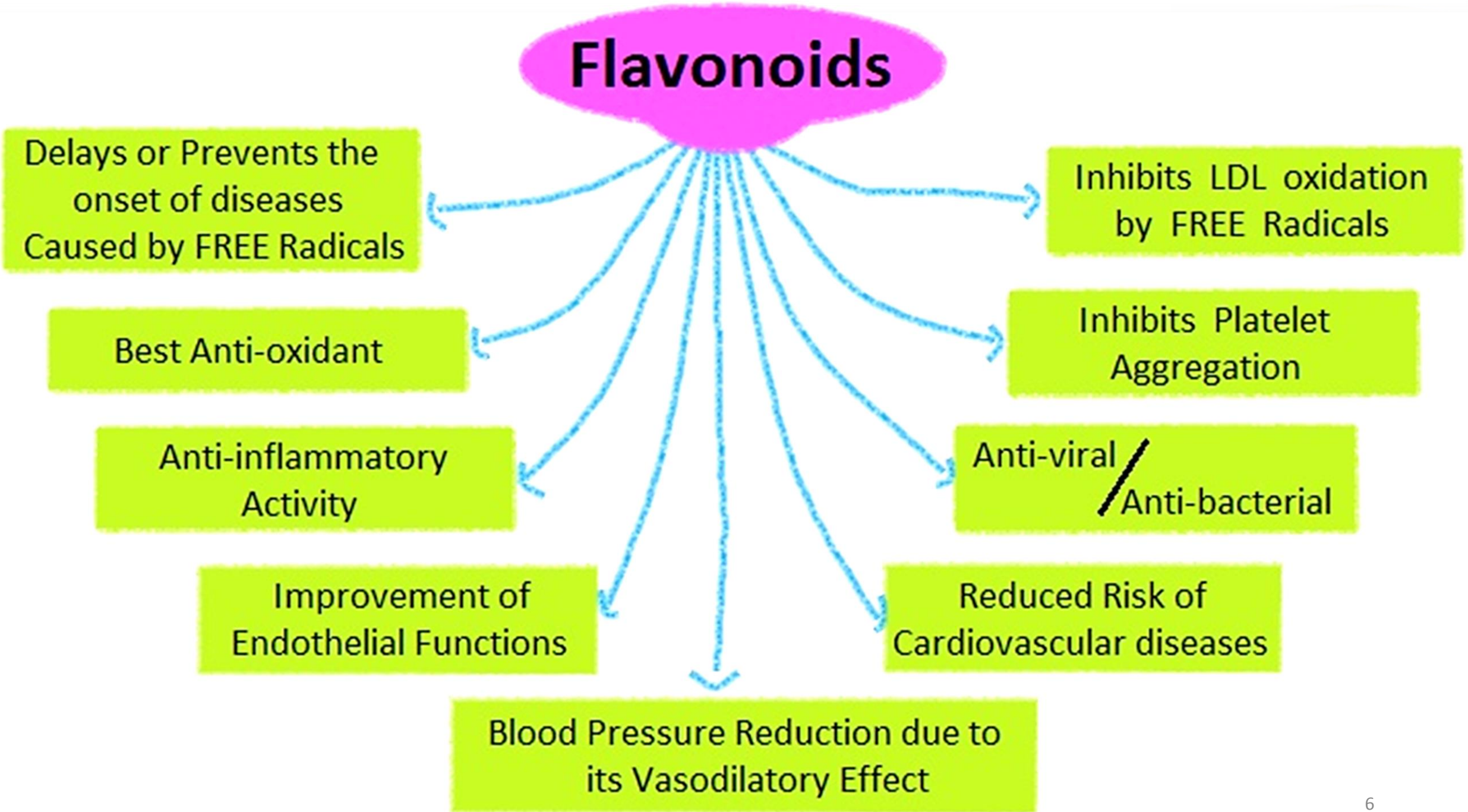
- The flavonoids are polyphenolic compounds possessing 15 carbon atoms; (1)
- two benzene rings joined by a linear three carbon chain having the carbon skeleton C6 - C3 - C6 (1)
- they are the plant pigments and they are having polar nature and is solouble in methanol and water. (2)



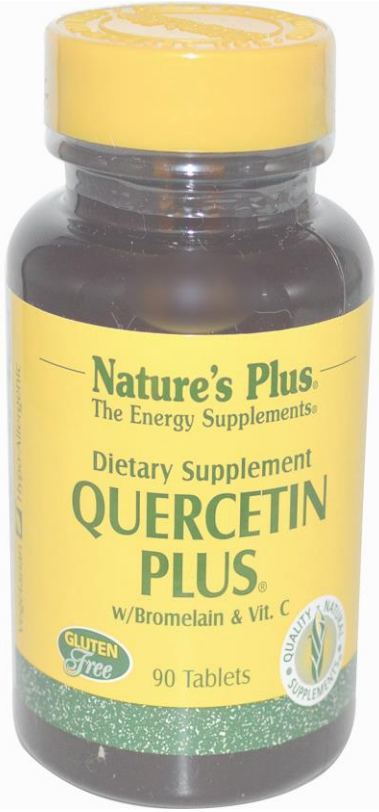
FLAVONOIDS

- Polyphenolic compounds that ubiquitous in nature (3)




Flavonoids
Delays or Prevents the onset of diseases Caused by FREE Radicals
Inhibits LDL oxidation by FREE Radicals
Best Anti-oxidant
Inhibits Platelet Aggregation
Anti-inflammatory Activity
Anti-viral / Anti-bacterial
Improvement of Endothelial Functions
Reduced Risk of Cardiovascular diseases
Blood Pressure Reduction due to its Vasodilatory Effect

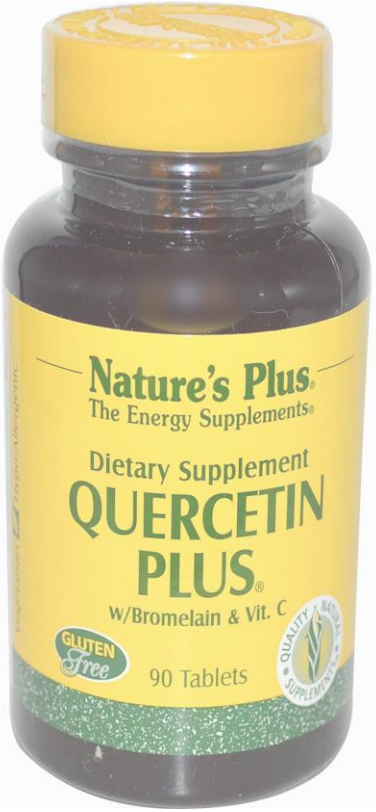
FLAVONOIDS



- Phenolics have been attributed with positive pharmacological properties. (4)

- having **antimutagenic** and **anticancerogenic** effects as well as being antioxidants. (5)

FLAVONOIDS



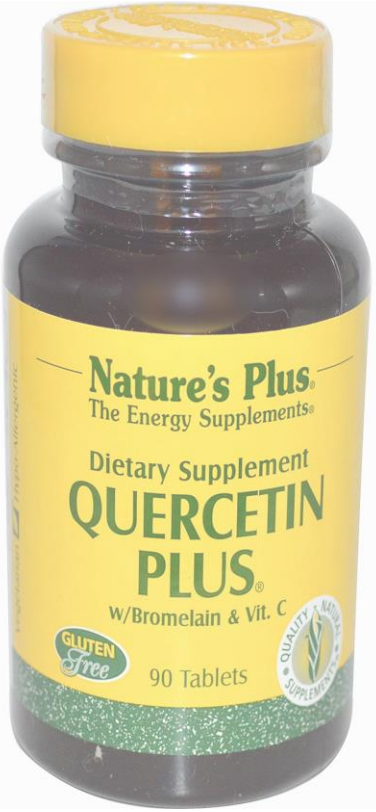
❖ *Bioavailability Problems (6)*

✓ **Poor absorption of flovonoids!!!**

✓1- Bacterial degradation of the phenol moiety of the molecule and a complex formation.

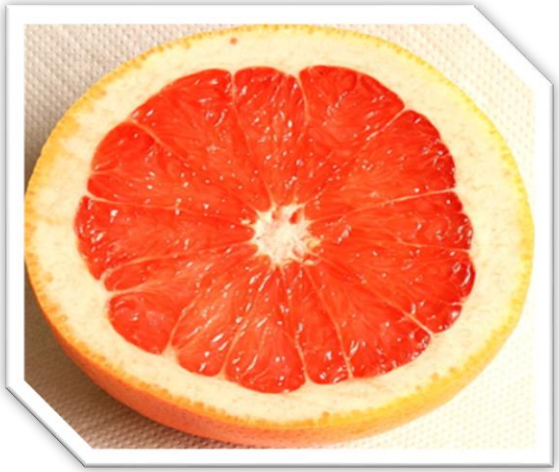
✓2- Flavonoid molecules have poor miscibility with lipids, which limited their ability to pass across the lipid-rich outer membranes of the small intestine.

FLAVONOIDS

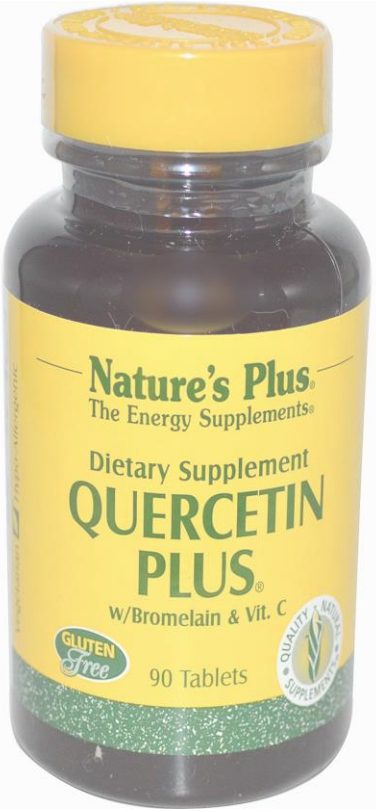


- constitute one of the most characteristic classes of compounds in higher plants. (7)

- Many flavonoids are easily recognised as flower pigments in most angiosperm families (**flowering plants**). (7)



FLAVONOIDS



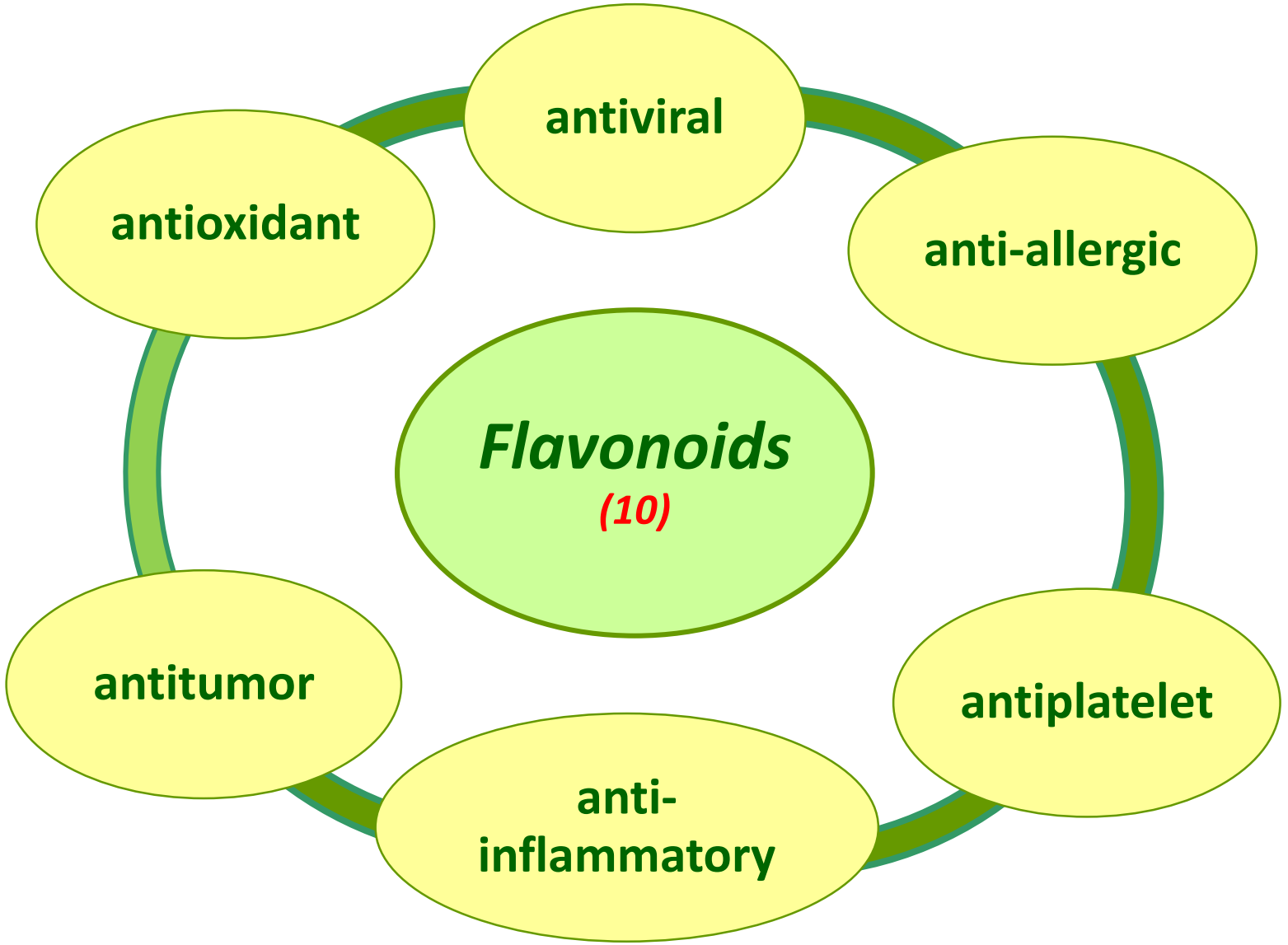
- However, their occurence is not restricted to flowers but include all parts of the plant.

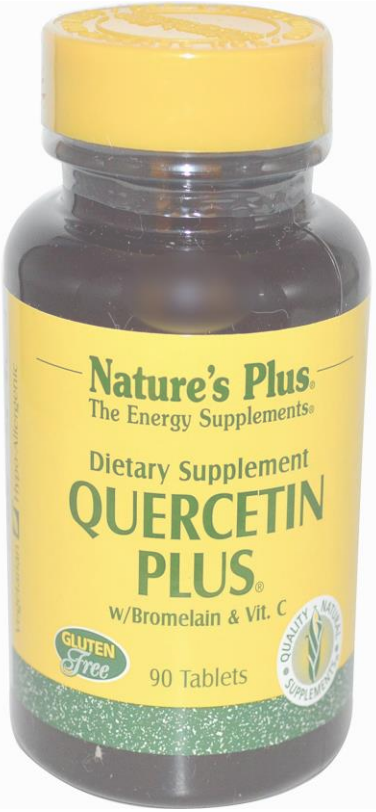
- They are secondary metabolite and effective in CNS disorders. (8)

FLAVONOIDS

- Some flavonoids in hops and beer have been found to have better antioxidant effects than tea or red wine.

- most flavonoids are found in fruits, vegetables, teas, and other drinks. (9)


antiviral
antioxidant
anti-allergic
Flavonoids
(10)
antitumor
antiplatelet
anti-
inflammatory

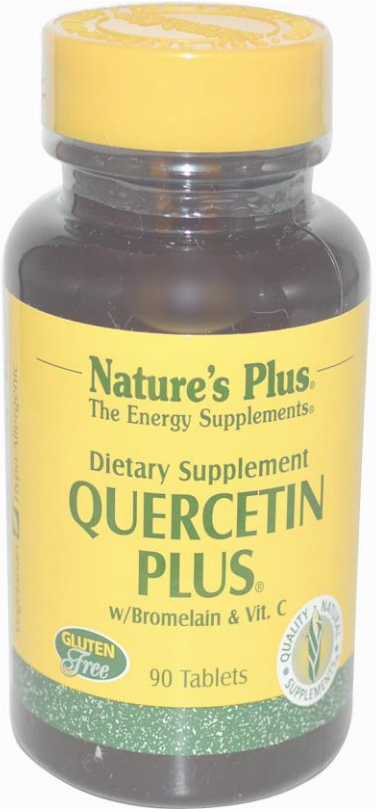

Nature's Plus
The Energy Supplements
Dietary Supplement
QUERCETIN
PLUS
w/Bromelain & Vit. C
GLUTEN Free
90 Tablets

QUERCETIN

- ***Boilogical Sources*** : **Quercetin** occurs in the bark of Quercus tinctoria belonging to family Hippocastanaceae. (11)

- **Quercetin** is a bioflavonoid (or flavonoid), which is a type pigment found in almost all herbs, fruits, and vegetables. (12)

QUERCETIN



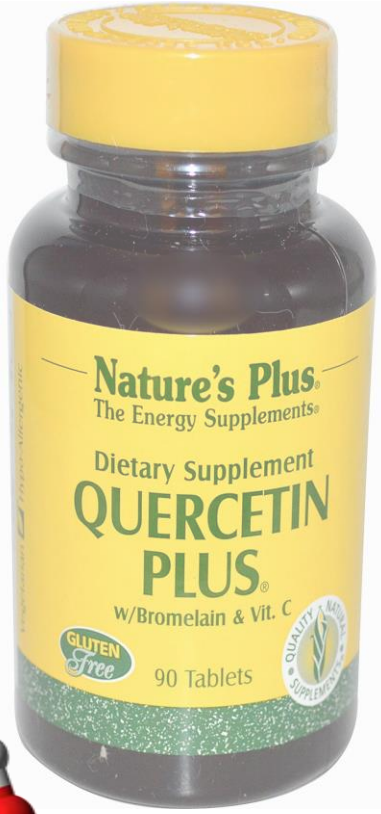
- Used for treating conditions of the heart and blood vessels,

including

- Atherosclerosis (13)
- high cholesterol (14)
- heart disease (15)
- circulation problems. (16)

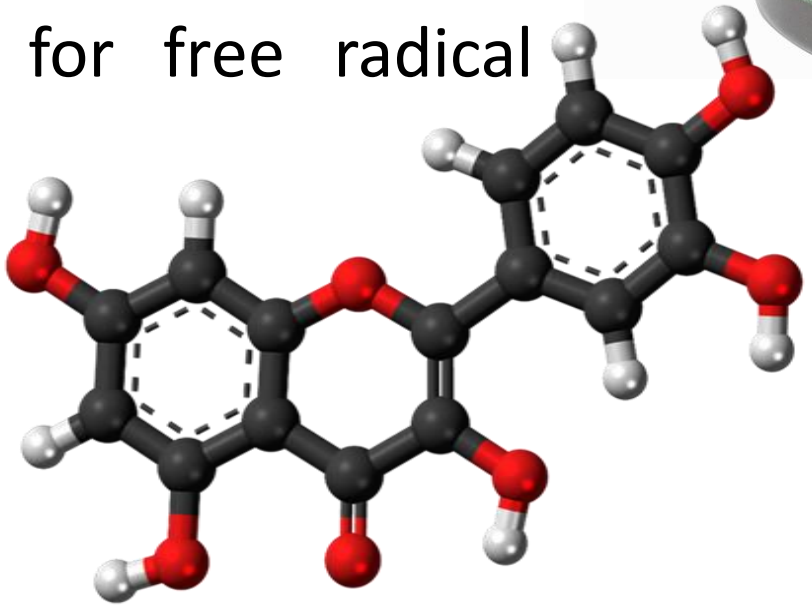
- ***Sources***: onions, apples, green and black teas and fruit skins
- Baking onions increases amount of quercetin.
- Boiling decreases amount of quercetin (17)

QUERCETIN

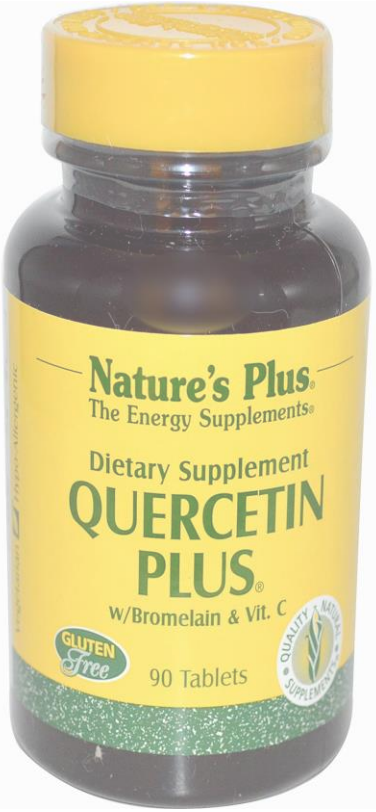


- the most abundant dietary flavonol, is a potent antioxidant. (18)

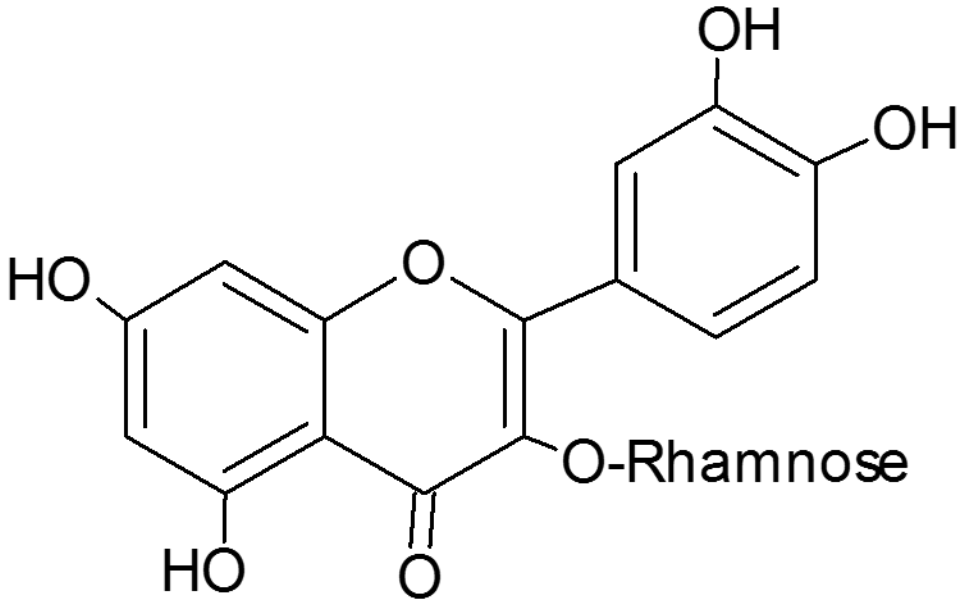
- it has all the right structural features for free radical scavenging activity. (19)



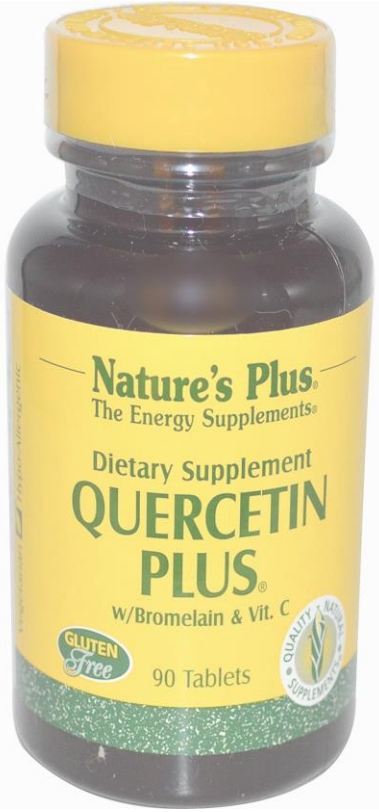
QUERCETIN



- Quercetin (3,3',4',5,7-pentahydroxyflavone). (20)
- This compound can be considered as a good candidate for anticancer therapy. (21)



QUERCETIN



- Behaving as antioxidant and/or prooxidant as well as modulating different intracellular signalling cascades may all play a certain role. (22)

- It has been suggested that these prooxidant capacities of quercetin could contribute to cancer chemotherapy and the inhibition of tumor growth. (23)

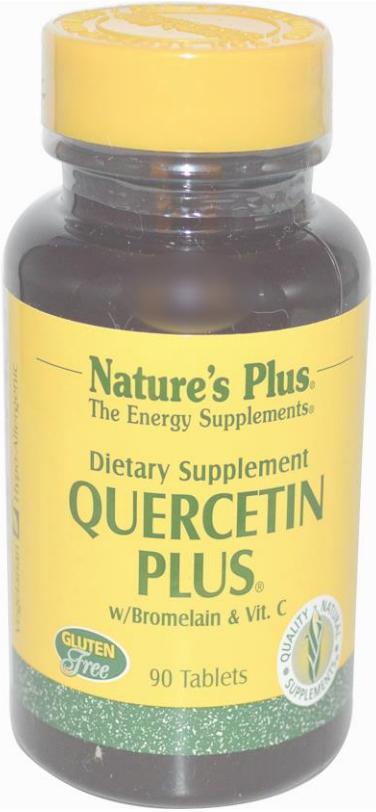
stimulate immune system

scavenge free radicals

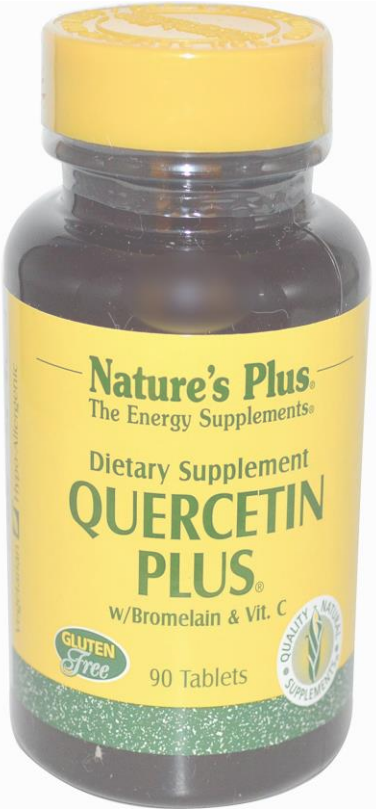
modulate enzyme activities (24)

alter the mitotic cycle

modify gene expression And induce apoptosis (25)



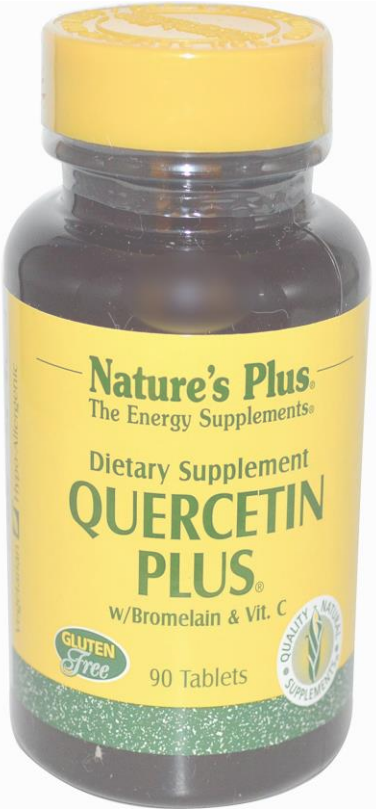
LITERATURE REVIEW



- Chan C-Y et al IN 2016: **Quercetin** treatment with 10 µM (half concentration of IC50) suppressed cell migration and invasion in EGFR-overexpressing HSC-3 and FaDu HNSCC cells. (26)

- Srivastava S et al IN 2016: **Quercetin** treatment in mice leads to lower tumor load, increased survival and minimal side effects. (27)

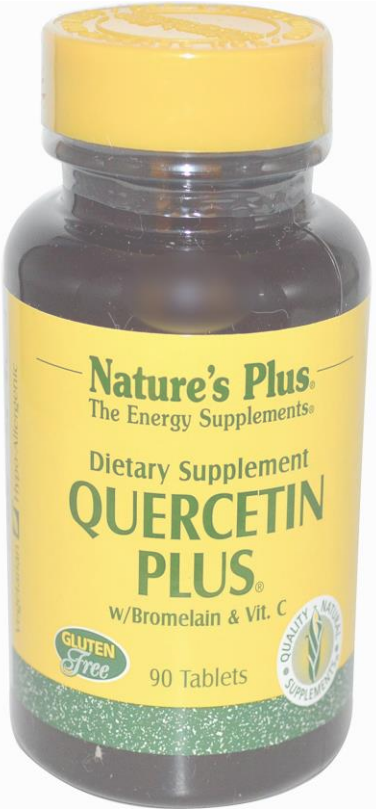
LITERATURE REVIEW



- Ranganathan S et al IN 2015: investigated the anti-proliferative effect of **quercetin** in two breast cancer cell lines(MCF-7andMDA-MB-231). (28)

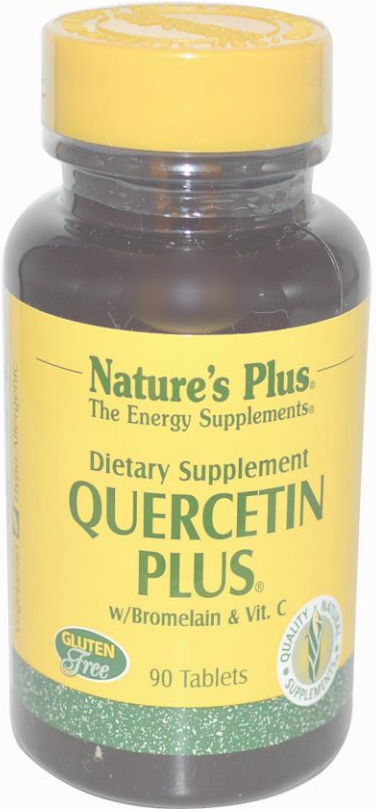
- Srinivasan A et al IN 2015: IC50 value (37µM) of **quercetin** showed significant cytotoxicity in MCF-7cells, which was not observed in MDA-MB-231cells even at 100µM of **quercetin** treatment. (29)

LITERATURE REVIEW



- IN 2013, 2012: **Quercetin** inhibits OSCC cell proliferation in a dose-dependent manner,Three doses (25,50 and 75µm) were chosen as test consentrations for the remainder of the experiments. (30,31)

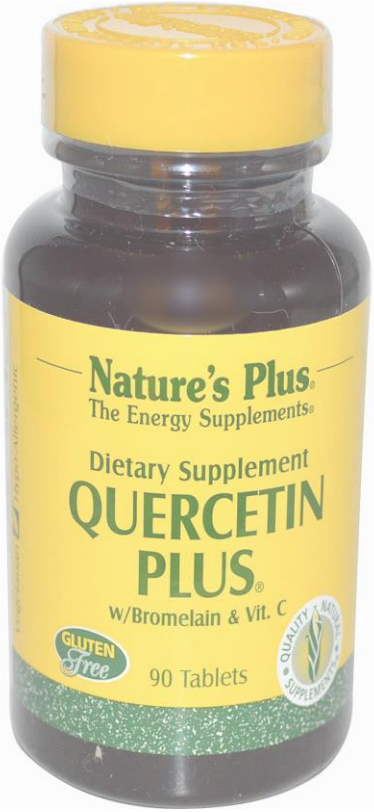
LITERATURE REVIEW



- Giri S et al IN 2011: Total **quercetin** derived from the diet is present in plasma at the nanomolar range (<100 nM).

- but can be increased to micromolar concentrations after supplementation.
- For example, 28 days of supplementation with 1 g/day of **quercetin** increased plasma concentrations to 1.5 µM. (32)

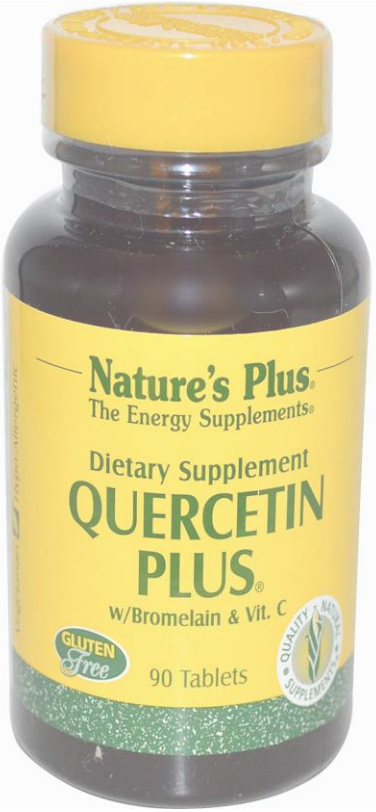
LITERATURE REVIEW



- **Quercetin** degraded the nuclear b-catenin and led to the inactivation of b-catenin downstream signaling. (32)
- Kawahara T et al in 2009: **Quercetin** Suppress the Growth of Leukemia and Lymphoma Cells.

- Cells were cultured in methylcellulose with 50 µM quercetin.
- **quercetin** colonization in cell lines HL-60 3% and Daudi cell lines was 0 %. (33)

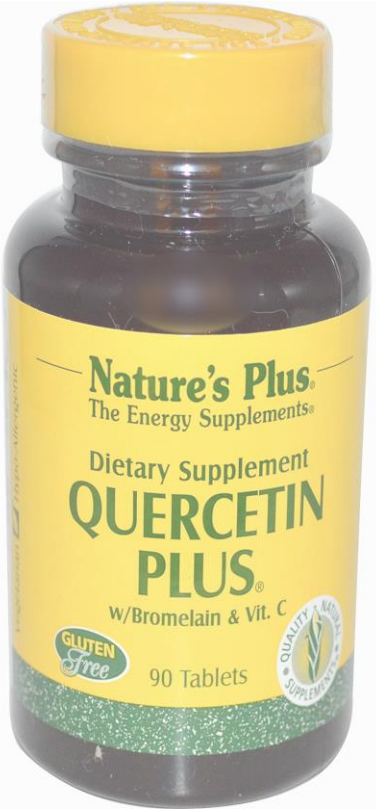
LITERATURE REVIEW



- In this study, concentrations of 25, 50 and 100 mg per kg of **quercetin** that injected via intra peritoneally into mice, and observed that increasing drug concentration can reduce the growth and proliferation. (33)

- Goya L et al IN 2006: **Quercetin** Induces Apoptosis via Caspase Activation, Regulation of Bcl-2, and Inhibition of PI-3-Kinase/Akt and ERK Pathways in a Human Hepatoma Cell Line (HepG2). (34)

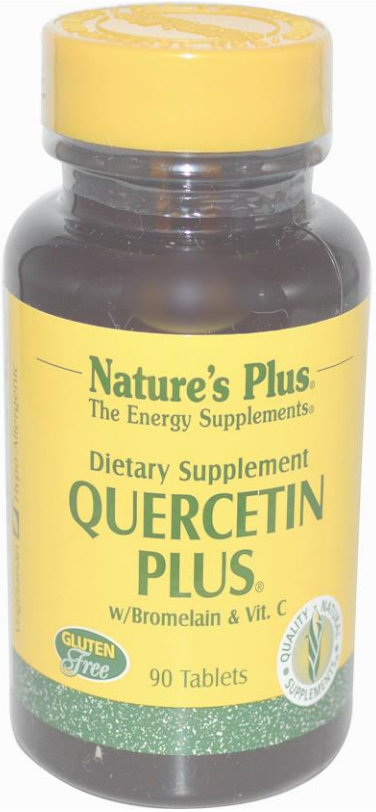
LITERATURE REVIEW



- Incubation with **quercetin** for 18 h displayed a dramatic cell mortality (68% with the highest concentration, 100 mmol/L, P , 0.05) with an estimated 50% of cell death (IC50) value of 87 mmol/L. (34)

- Walle T et al IN 2005: this study examed Antiproliferative effects of **quercetin** in SCC-9 cells,
- Observed that the growth of SCC-9 cells at a concentration of 100 µmol per liter quercetin more decrease with compared to concentrations of 10 µm per liter . (35)

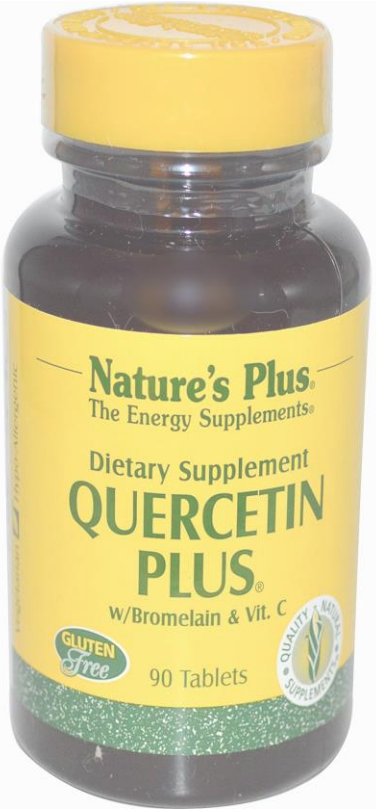
LITERATURE REVIEW



- Elattar TM et al IN 1999: **Quercetin** exhibited a biphasic effect, stimulation at 1.0 and 10 µmol and minimal inhibition at 100 µmol in cell growth and DNA synthesis. (36)

- Combining 50 µmol of resveratrol with 10, 25 and 50 µmol of quercetin resulted in gradual and significant increase in the inhibitory effect of the two compounds. (36)

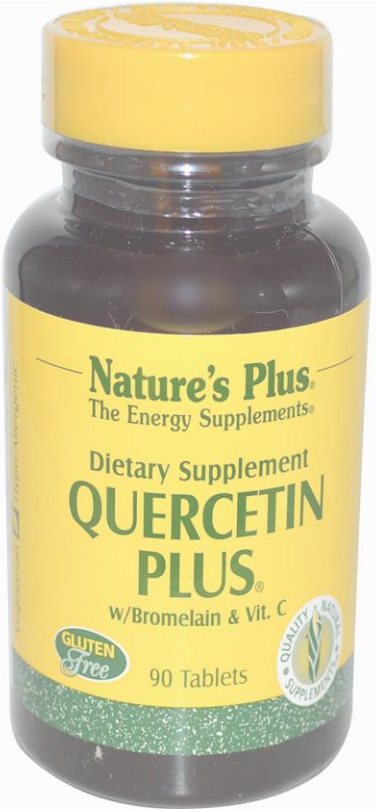
RESULTS



- ***Flavonoids*** are widely distributed among various plants and in foodstuffs; consequently, they constitute an unavoidable component of the diet.

- Flavonoids like ***quercetin*** have potential as starting material in drug development pro- grammes.

RESULTS

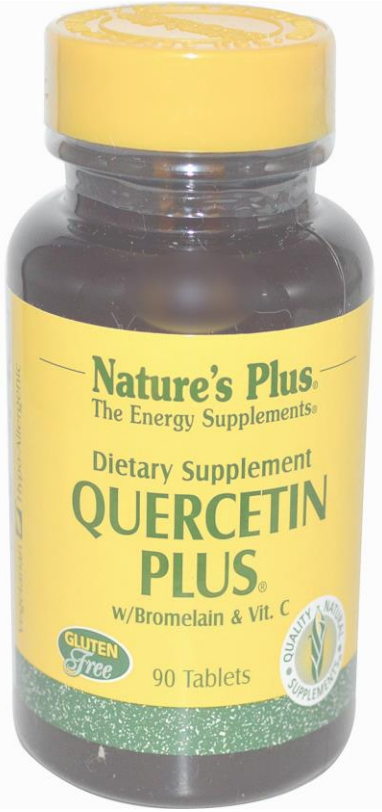


- the development of experimental ***anticancer*** flavonoid derivatives.

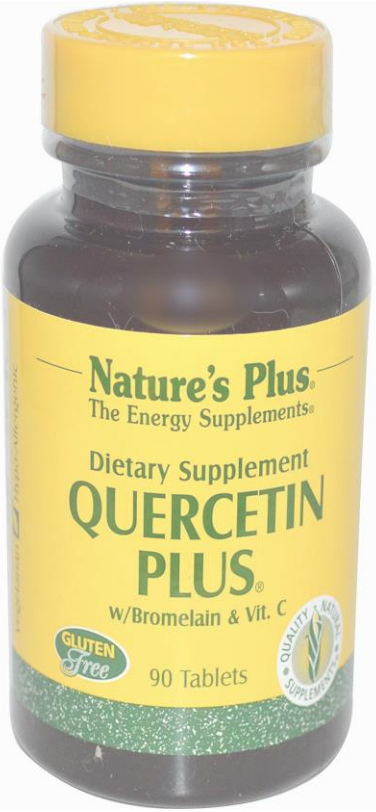
- A similar approach could result in the development of effective ***antiplatelet, antiviral and anti-inflammatory*** agents.

REFRENCES

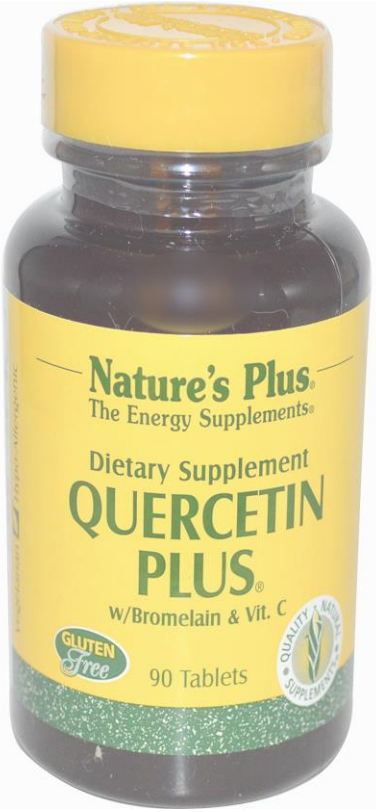
- 1. Aksoy M, Gülçin İ, Küfrevioğlu Öİ, editors. In vitro antioxidant profiles of some flavonoids. INTERNATIONAL CONFERENCE ON ADVANCES IN NATURAL AND APPLIED SCIENCES: ICANAS 2016; 2016: AIP Publishing.
- 2. Dower JI, Geleijnse JM, Gijsbers L, Schalkwijk C, Kromhout D, Hollman PC. Supplementation of the pure flavonoids epicatechin and quercetin affects some biomarkers of endothelial dysfunction and inflammation in (pre) hypertensive adults: a randomized double-blind, placebo-controlled, crossover trial. The Journal of nutrition. 2015;145(7):1459-63.
- 3. Feucht W, Schmid M, Treutter D. Acclimation Changes of Flavonoids in Needles of Conifers during Heat and Drought Stress 2015. Climate. 2016;4(3):35.
- 4. Garcia-Castello EM, Rodriguez-Lopez A, Mayor L, Ballesteros R, Conidi C, Cassano A. Optimization of conventional and ultrasound assisted extraction of flavonoids from grapefruit (Citrus paradisi L.) solid wastes. LWT-Food Science and Technology. 2015;64(2):1114-22.
- 5. Havsteen BH. The biochemistry and medical significance of the flavonoids. Pharmacology & therapeutics. 2002;96(2):67-202.



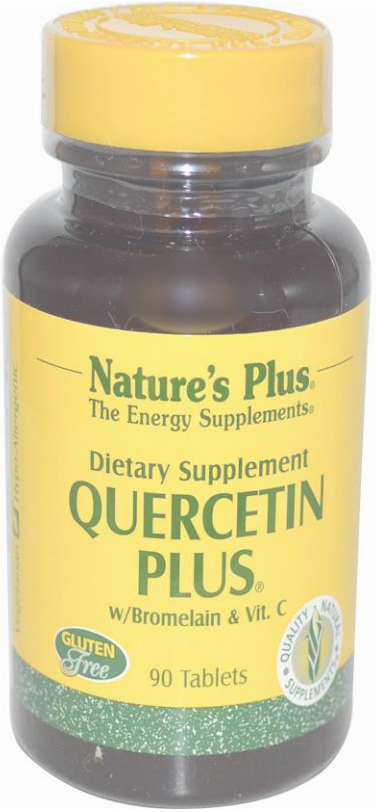
- 6. Hertog MG, Feskens EJ, Kromhout D, Hollman P, Katan M. Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. The Lancet. 1993;342(8878):1007-11.
- 7. McKay DL, Chen C-YO, Zampariello CA, Blumberg JB. Flavonoids and phenolic acids from cranberry juice are bioavailable and bioactive in healthy older adults. Food chemistry. 2015;168:233-40.
- 8. Mena P, Cirlini M, Tassotti M, Herrlinger KA, Dall'Asta C, Del Rio D. Phytochemical Profiling of Flavonoids, Phenolic Acids, Terpenoids, and Volatile Fraction of a Rosemary (Rosmarinus officinalis L.) Extract. Molecules. 2016;21(11):1576.
- 9. Middleton E, Kandaswami C, Theoharides TC. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. Pharmacological reviews. 2000;52(4):673-751.
- 10. Scalbert A, Zamora-Ros R. Bridging evidence from observational and intervention studies to identify flavonoids most protective for human health. The American journal of clinical nutrition. 2015;101(5):897-8.
- 11. Bakkialakshmi S, Roy J. ANALYSIS OF INTERACTION OF HUMAN HEMOGLOBIN WITH QUERCETIN: FLUORESCENCE SPECTROSCOPIC AND MOLECULAR MODELING APPROACH. 2016.



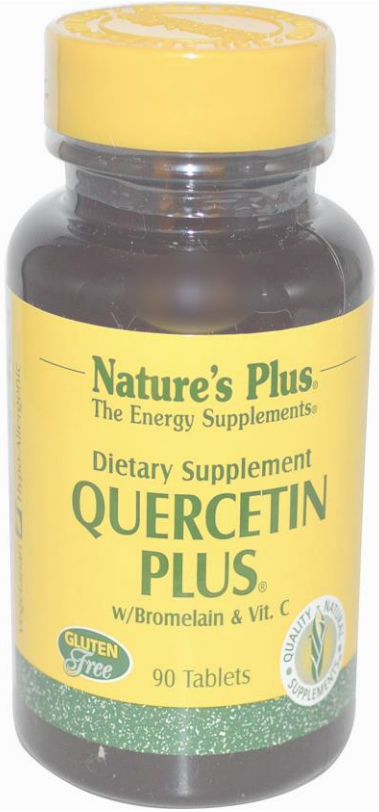
- 12. Petersen B, Egert S, Bosy-Westphal A, Müller MJ, Wolffram S, Hubbermann EM, et al. Bioavailability of quercetin in humans and the influence of food matrix comparing quercetin capsules and different apple sources. Food Research International. 2016.
- 13. Brüll V, Burak C, Stoffel-Wagner B, Wolffram S, Nickenig G, Müller C, et al. No effects of quercetin from onion skin extract on serum leptin and adiponectin concentrations in overweight-to-obese patients with (pre-) hypertension: a randomized double-blinded, placebo-controlled crossover trial. European Journal of Nutrition. 2016:1-11.
- 14. Prasain J, Rajbhandari R, Keeton A, Piazza G, Barnes S. Cellular Metabolism Of Quercetin And Its Analogs In Bladder Cancer Cells. Planta Medica. 2016;82(05):OA37.
- 15. Smith C, Lombard KA, Peffley EB, Liu W. Genetic analysis of quercetin in onion (Allium cepa L.)'Lady Raider'. Texas Journal of Agriculture and Natural Resources. 2016;16:24-8.
- 16. Toumi ML, Merzoug S, Tahraoui A. Effects of quercetin on predator stress-related hematological and behavioural alterations in pregnant rats and their offspring. Journal of biosciences. 2016;41(2):237-49.
- 17. Jain J, Chaurasiya N, Nanayakkara N, McChesney J, Walker L, Tekwani B. Quercetin Potentiates Toxicity Of Hemolytic Drugs In G6PD Deficient Human Erythrocytes. Planta Medica. 2016;82(05):PB17.
- 18. Limtrakul P, Khantamat O, Pintha K. Inhibition of P-glycoprotein function and expression by kaempferol and quercetin. Journal of chemotherapy. 2013.



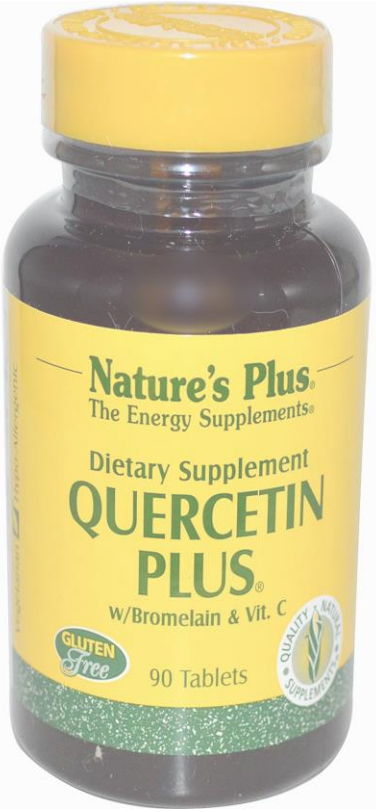
- 19. Gharat SA, Momin M, Bhavsar C. Oral Squamous Cell Carcinoma: Current Treatment Strategies and Nanotechnology-Based Approaches for Prevention and Therapy. Critical Reviews™ in Therapeutic Drug Carrier Systems. 2016;33(4).
- 20. Jahan S, Iftikhar N, Ullah H, Rukh G, Hussain I. Alleviative effect of quercetin on rat testis against arsenic: a histological and biochemical study. Systems biology in reproductive medicine. 2015;61(2):89-95.
- 21. M Alvarez-Suarez J, Giampieri F, Battino M. Honey as a source of dietary antioxidants: structures, bioavailability and evidence of protective effects against human chronic diseases. Current medicinal chemistry. 2013;20(5):621-38.
- 22. Mijares MR, Ochoa M, Barroeta A, Martinez GP, Suarez AI, Compagnone RS, et al. Cytotoxic effects of Fisturalin-3 and 11-Deoxyfisturalin-3 on Jurkat and U937 cell lines. Biomedical Papers. 2013;157(3):222-6.
- 23. Sak K. The Val158Met Polymorphism in COMT Gene and Cancer Risk: Role of Endogenous and Exogenous Catechols. Drug Metabolism Reviews. 2016(just-accepted):1-46.
- 24. Steiner J, Davis J, McClellan J, Enos R, Carson J, Fayad R, et al. Dose-dependent benefits of quercetin on tumorigenesis in the C3 (1)/SV40Tag transgenic mouse model of breast cancer. Cancer biology & therapy. 2014;15(11):1456-67.
- 25. Upadhyay RK. Nutraceutical, pharmaceutical and therapeutic uses of Allium cepa: A review. International Journal of Green Pharmacy (IJGP). 2016;10(1).



- 26. Chan C-Y, Lien C-H, Lee M-F, Huang C-Y. Quercetin suppresses cellular migration and invasion in human head and neck squamous cell carcinoma (HNSCC). BioMedicine. 2016;6(3).
- 27. Srivastava S, Somasagara RR, Hegde M, Nishana M, Tadi SK, Srivastava M, et al. Quercetin, a Natural Flavonoid Interacts with DNA, Arrests Cell Cycle and Causes Tumor Regression by Activating Mitochondrial Pathway of Apoptosis. Scientific reports. 2016;6
- 28. Ranganathan S, Halagowder D, Sivasithambaram ND. Quercetin Suppresses Twist to Induce Apoptosis in MCF-7 Breast Cancer Cells. PloS one. 2015;10(10):e0141370.
- 29. Srinivasan A, Thangavel C, Liu Y, Shoyele S, Den RB, Selvakumar P, et al. Quercetin regulates β-catenin signaling and reduces the migration of triple negative breast cancer. Molecular carcinogenesis. 2015.
- 30. Chen S-F, Nien S, Wu C-H, Liu C-L, Chang Y-C, Lin Y-S. Reappraisal of the anticancer efficacy of quercetin in oral cancer cells. Journal of the Chinese medical association. 2013;76(3):146-52.
- 31. Spagnuolo C, Russo M, Bilotto S, Tedesco I, Laratta B, Russo GL. Dietary polyphenols in cancer prevention: the example of the flavonoid quercetin in leukemia. Ann N Y Acad Sci. 2012;1259:95-103.
- 32. Mazumdar M, Giri S, Giri A. Role of quercetin on mitomycin C induced genotoxicity: analysis of micronucleus and chromosome aberrations in vivo. Mutat Res. 2011;721(2):147-52.
- 33. Kawahara T, Kawaguchi-Ihara N, Okuhashi Y, Itoh M, Nara N, Tohda S. Cyclopamine and quercetin suppress the growth of leukemia and lymphoma cells. Anticancer research. 2009;29(11):4629-32.



- 34. Granado-Serrano AB, Martín MA, Bravo L, Goya L, Ramos S. Quercetin induces apoptosis via caspase activation, regulation of Bcl-2, and inhibition of PI-3-kinase/Akt and ERK pathways in a human hepatoma cell line (HepG2). The Journal of nutrition. 2006;136(11):2715-21.
- 35. Browning AM, Walle UK, Walle T. Flavonoid glycosides inhibit oral cancer cell proliferation--role of cellular uptake and hydrolysis to the aglycones. The Journal of pharmacy and pharmacology. 2005;57(8):1037-42.
- 36. Elattar TM, Virji AS. The effect of red wine and its components on growth and proliferation of human oral squamous carcinoma cells. Anticancer research. 1999;19(6b):5407-14.




THANK YOU